



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
|-----------------|-------------|----------------------|---------------------|------------------|

10/766,086

01/27/2004

Ashvinikumar V. Gavai

LA0074 NP

2426

23914

7590

04/27/2005

STEPHEN B. DAVIS  
BRISTOL-MYERS SQUIBB COMPANY  
PATENT DEPARTMENT  
P O BOX 4000  
PRINCETON, NJ 08543-4000

EXAMINER

PAVIGLIANITI, ANTHONY JOSEPH

ART UNIT

PAPER NUMBER

1626

DATE MAILED: 04/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/766,086

Applicant(s)

GAVAI ET AL.

Examiner

Anthony J. Paviglianiti

Art Unit

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-13 are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)             | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. ____.  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date ____.   | 6) <input type="checkbox"/> Other: ____.                                    |

### DETAILED ACTION

**Claims 1 – 13** are currently pending in the instant application and are subject to the following restriction.

#### **Election/Restrictions**

The Markush groups set forth in the claims include both independent and distinct inventions, and patentably distinct compounds (or species) within each invention. However, this application discloses and claims a plurality of patentably distinct inventions far too numerous to list individually. Moreover, each of these inventions contains a plurality of patentably distinct compounds, also far too numerous to list individually. **For these reasons provided below, restriction to one of the following inventions is required under 35 U.S.C. 121**, wherein an Invention is a set of patentably distinct inventions of a broad statutory category (e.g., compounds, methods of use, methods of making, etc.):

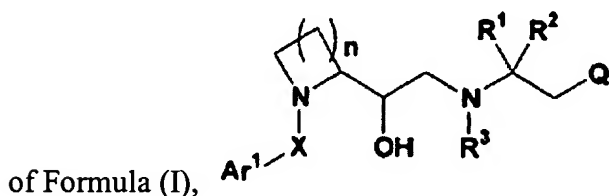
- I. Claims 1 – 7**, drawn to products of formula (I), classified in class 546, subclasses 174 and 176, and other subclasses.
- II. Claims 9 –11**, drawn to methods of use of products of formula (I), classified in class 514, subclass 314, and other subclasses.
- III. Claims 8, 12 and 13**, drawn to compositions comprising products of formula (I) plus additional therapeutic agents (such as MMP inhibitors or modulators of bone resorption), or compounds of formula (I) which modulate the calcium sensing receptor, as classified in: class 546, subclass 174; class 514, subclass 314; and in other classes and subclasses.

Art Unit: 1626

**In addition to an election of one of the above Groups, restriction is further required under 35 U.S.C. §121 as follows:**

In accordance with the decisions in In re Harnisch, 631 F.2d 716, 206 USPQ 300 (CCPA 1980) and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App & Int. 1984), restriction of a Markush group is proper where the compounds with the group either (1) do not share a common utility, or (2) do not share a substantial structural feature disclosed as being essential to that utility. In addition, a Markush group may encompass a plurality of independent and distinct inventions where two or more members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the claim obvious under 35 U.S.C. §103 with respect to the other member(s).

Whether **Group I, II, or III** is elected, **an election of a single compound is further required**, including an exact definition of each substitution on the base molecule [Formula (I)], where a single member at each substituent group is selected. For example, if the base molecule



recited to be “a substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl,” then applicant must select a single substituent representing  $\text{Ar}^1$ , such as a “quinoline” group, as well as its substituents, such as -Cl and -OH (as in **Claim 6**, species #2, on page 121, line 4); and also specific values at each subsequent variable position ( $\text{X}$ ,  $n$ ,  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{Q}$ ,  $\text{G}$ ,  $m$ ,  $\text{R}^4$ ,  $\text{R}^5$ ,  $\text{R}^6$ ,  $z$ , etc.), so that a single compound is identified.

Art Unit: 1626

One suggestion for the election of a single compound would be to select one from the lists of compounds in **Claim 5** or **Claim 6**; or, alternatively, to select one of the compounds disclosed as Examples 1 – 231 on pages 37 – 114 of the Specification.

If **Group II** is elected, then **election of a specific method of use, *along with an elected compound of formula (I)*, is required**; for example, a method of treating:

- A. hypoparathyroidism;
- B. osteosarcoma;
- C. fracture healing;
- D. periodontal disease;
- E. Paget's disease;
- F. osteopenia; or
- G. metastatic bone disease;

etc., using an elected compound of formula (I).

In the instant case, upon election of a single compound, the Office will review the claims and disclosure to determine the scope of the independent invention encompassing the elected compound (compounds which are so similar as to be within the same inventive concept and reduction to practice). The scope of an independent invention will encompass all compounds within the scope of the claim which fall into the same class and subclass as the elected compound, but may also include additional compounds which fall in related subclasses.

Examination will then proceed on the elected compound *and* the entire scope of the invention encompassing the elected compound as defined by common classification. A clear

Art Unit: 1626

statement of the examined invention, defined by those class(es) and subclass(es) will be set forth in the first action on the merits.

Note that the restriction requirement will not be made final until such time as Applicant is informed of the full scope of compounds along with (if appropriate) the process of using or making the compounds under investigation. This will be set forth by reference to specific class(es) and subclass(es) examined.

Should Applicant traverse on the ground that the compounds are not patentably distinct, Applicant should submit evidence or identify such evidence now of record showing the compounds to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. §103(a) of the other invention.

All compounds falling outside of the class(es) and subclass(es) of the selected compound and any other subclass encompassed by the election above will be directed to non-elected subject matter and will be withdrawn from consideration under 35 U.S.C. §121 and 37 C.F.R. §1.142(b). Applicant may reserve the right to file divisional applications on the remaining subject matter. The provisions of 35 U.S.C. §121 apply with regard to double patenting covering divisional applications.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. §1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 C.F.R. §1.48(b) and by the fee required under 37 C.F.R. §1.17(i).

Art Unit: 1626

If desired upon election of a single compound, applicants can review the claims and disclosure to determine the scope of the invention and can set forth a group of compounds which are so similar within the same inventive concept and reduction to practice. Markush claims must be provided with support in the disclosure for each member of the Markush group. See MPEP §608.01(p). Applicant should exercise caution in making a selection of a single member for each substituent group on the base molecule to be consistent with the written description.

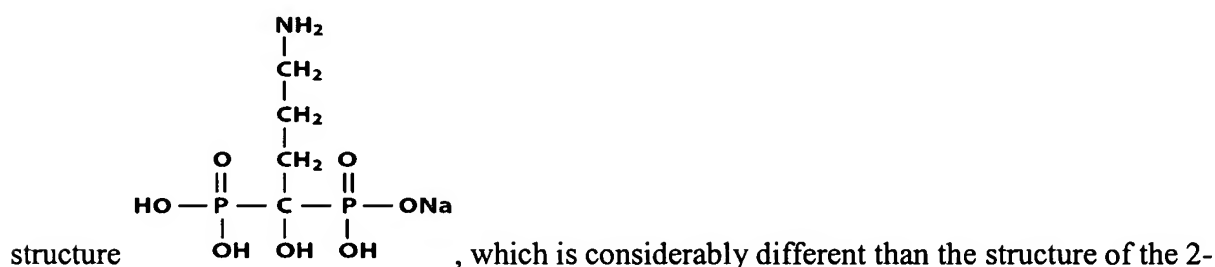
**Rationale Establishing Patentable Distinctiveness Within Each Group**

Each Group listed above is directed to or involves the use of compounds which are recognized in the art as being distinct from one another because of their diverse chemical structure, their different chemical properties, modes of action, different effects and reactive conditions (MPEP §806.04, MPEP §808.01). Additionally, the level of skill in the art is not such that one invention would be obvious over the other invention (Group); i.e., they are patentable over each other. Chemical structures which are similar are presumed to function similarly, whereas chemical structures that are not similar are not presumed to function similarly. The presumption even for similar chemical structures though is not irrebuttable, but may be overcome by scientific reasoning or evidence showing that the structure of the prior art would not have been expected to function as the structure of the claimed invention. Note that in accordance with the holding of Application of Papesch, 50 CCPA 1084, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) and In re Lalu, 223 USPQ 1257 (Fed. Cir. 1984), chemical structures are patentably distinct where the structures are either not structurally similar, or the prior art fails to suggest a function of a claimed compound would have been expected from a similar structure.

Art Unit: 1626

**The above Groups represent general areas wherein the inventions are independent and distinct, each from the other, because of the following reasons:**

**Group I** and **Group II** are related as product and method of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially-different process of using that product. MPEP §806.05(h). Applying this rule to the instant case, the method for using the products as claimed – as a treatment for Paget’s disease, for example – can be practiced with a materially different product, such as the compound alendronate, a bisphosphonate compound with the chemical



substituted cyclic amines of the present invention. See Delmas, P. and Meunier, P., “The Management of Paget’s Disease of Bone,” N. Engl. J. Med., vol. 336(8), pages 558-566 (Feb. 20, 1997) at p. 563, col. 1, lines 10 – 22, and p. 561, Table1.

**Group I** and **Group III** are separate and distinct inventions from each other because **Group I** is comprised of compounds of formula (I) and pharmaceutical compositions of a single compound of formula (I) plus a carrier, while **Group III** requires combination with at least one additional therapeutic agent (such as anti-osteoporosis agents, modulators of bone resorption, selective androgen receptor modulators, MMP inhibitors, or other compounds of formula (I)), or compositions having an intended use which imparts an additional limitation (modulating the



Art Unit: 1626

calcium sensing receptor) such that a prior art reference to one invention (Group) would not anticipate or render obvious the other, and they are patentable over each other.

**Group II** and **Group III** are also related as method of use and product. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially-different process of using that product. MPEP §806.05(h). In this instance, as was demonstrated earlier, the method of treating one of the claimed diseases in **Group II** – Paget’s disease, for example – can be practiced with gallium nitrate, which is a materially-different product than the compositions in **Group III** of the present invention, which are combinations of cyclic amines and other therapeutic agents. See Delmas, P. and Meunier, P., “The Management of Paget’s Disease of Bone,” N. Engl. J. Med., vol. 336(8), pages 558-566 (Feb. 20, 1997) at p. 560, col. 2, lines 24 - 28 (gallium nitrate).

In addition, because of the number of classes and subclasses in each of the Groups, a serious burden is imposed upon the examiner to perform a complete search of the defined areas. Therefore, for the reasons given above, the restriction set forth is proper, and not to restrict would impose a serious burden in the examination of this application.

#### **Advisory of Rejoinder**

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

Art Unit: 1626

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

**During a telephone conversation with Maureen O'Brien, Esq., on March 28, 2004, the restriction requirements were discussed, but applicant did not elect by telephone.**

Applicant is advised that the reply to this requirement to be complete must include an election of the Invention to be examined even though the requirement be traversed. 37 C.F.R. §1.143.

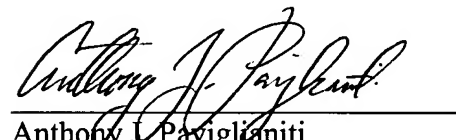
Applicant is further advised that a reply to this requirement must identify the specific compound that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.


### **Conclusion**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Anthony J. Paviglianiti** whose telephone number is **(571) 272-3107**. The examiner can normally be reached on Monday-Friday, 8:30 a.m. - 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane, may be reached at (571) 272-0699. **The FAX phone number for the organization where this application or proceeding is assigned is (571) 273-8300. Please note that this is a new central FAX number for all official correspondence.**

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
\_\_\_\_\_  
Anthony J. Paviglianiti  
Patent Examiner  
TC-1600, Art Unit 1626

  
\_\_\_\_\_  
for Joseph K. McKane  
Supervisory Patent Examiner  
TC-1600, Art Unit 1626